b. <u>Cephalometric Outcomes of Skeletal Morphology</u>

1) ***Example of Request Application for IRB approval*** – For all aspects of inter-center comparisons, participating Centers must obtain IRB approval. An example of such a request that has been used successfully in Americleft is provided in APPENDIX 7 which was an addendum to the IRB request for approval of the dental arch relationship part of the project (APPENDIX 2). Please note that it again includes a request to waive specific informed consent from the patients. Depending on the sample you may be using (current patients vs. historical records) and depending on the agreeability of your IRB, this may or may not be accepted and especially for more current or even prospectively gathered records, may not be suitable and specific informed consent might be necessary for the outcome audit. Also it is important to stress that if your protocol for mixed dentition orthodontic treatment planning includes routine taking of lateral cephalometric radiographs the use of those for outcome audit purposes and the fact that the radiographs can be totally void of any PHI for use in the audits, that you may be able to get approval without additional informed consent as long as parents had already given informed consent when they started orthodontic treatment planning and treatment. This may be especially true if the outcomes from an historical sample at your Center are the ones you will be investigating.

2) ***Sample* - Teams interested in participating should adhere to the following Sample Inclusion / Exclusion criteria**

   ✓ **Inclusion Criteria:**
   - Caucasian subjects with a history of non-syndromic complete unilateral cleft lip and palate, (diagnosis confirmed by neonatal photographs, study models, and/or a clearly written preoperative description)
   - Patients with Simonart's bands will be included, provided no hard tissue union exists
   - Patients must have lateral cephalograms (with the teeth in occlusion) available at the approximate age of 9 years (range 7-11 years)
   - Each subject has received all of his/her primary surgery and previous care in the Institution concerned.
   - Consecutively treated cases are required

   ✓ **Exclusion Criteria:**
   - Patients with associated anomalies or syndromes.
   - Patients with incomplete clefts (other than a Simonart's band).
   - Patients who have had any (fixed- or removable-appliance) orthodontic treatment, maxillary expansion, headgear or face-mask therapy prior to taking the cephalometric radiographs
   - Patients that have undergone any orthognathic surgery or osteodistraction treatment prior to taking the cephalometric radiographs

3) ***Descriptive Data* -** As per the original Eurocleft Study (Shaw *et al.*, 1992), the following descriptive data will be collected for patients included within the investigation (APPENDIX 8):

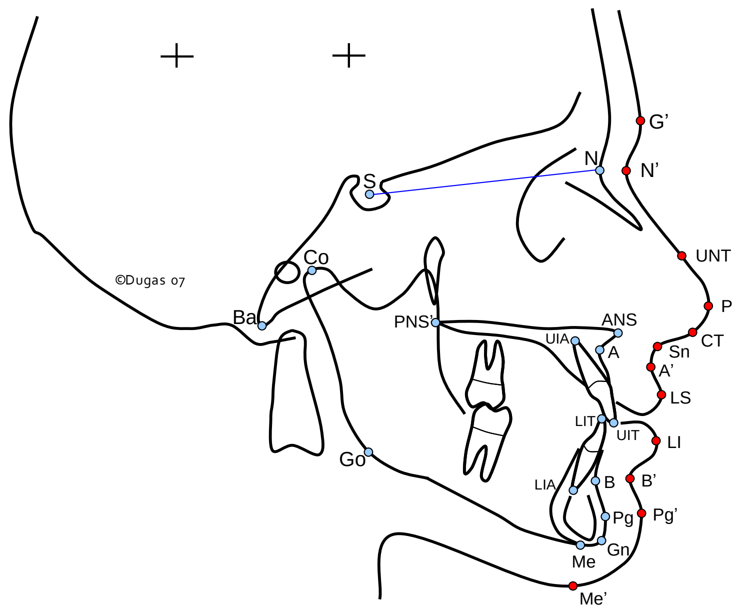
   ✓ Date of birth

- ✓ Sex
- ✓ Side of cleft
- ✓ Presence of Simonart's band
- ✓ How the diagnosis was confirmed
- ✓ Date of lateral cephalogram
- ✓ Age at lateral cephalogram
- ✓ Age and date of alveolar bone grafting procedure, if performed
- ✓ Whether or not infant orthopedics was performed
- ✓ Other surgical procedures undergone
- ✓ Code(s) representing surgeon(s) who performed each procedure (in the case of multiple surgeons at the same Institution)

Additionally, a thorough description of each Center's surgical treatment protocol will be recorded including the technique/type of lip repair, the technique/type of palatal closure, the technique/type of alveolar bone graft (and whether primary or secondary) if performed, and the approximate age of the patient(s) at the time of operation (APPENDIX 1).

4) ***Methods*** **-** The investigator performing the assessment will be blind to these data (including the origin of the lateral cephalogram). Different investigators will perform the final evaluation of the numerical data for the synthesis of the discussion. If the records submitted are not in DICOM or JPEG format, a film scanner (Epson model #1680) will be used to convert them into JPEG format for cephalometric analysis. The radiographs from each CLP center will be digitized using Dentofacial Planner version 8.0 cephalometric software (http://www.dentofacial.com/). Sixteen hard tissue and twelve soft tissue landmarks will be used. Each cephalometric landmark will be identified twice, by two independent examiners. A number of hard-tissue and soft-tissue cephalometric variables per radiograph will be calculated (Tables I). The mean of the numerical outcomes per cephalometric measurement will be used for the intercenter cephalometric comparison. The linear distance Ba-N (Basion-Nasion) in mm will be used for size adjustment of all linear measurements. The cephalometric assessment will be performed at the Division of Orthodontics, The Hospital for Sick Children, Toronto, Canada; and at the Department of Orthodontics, Faculty of Dentistry, University of Toronto, Toronto, Canada.

FIGURE 1: Reference landmarks on the lateral cephalometric tracing



The following Table is the list of measurements that will be taken for comparison between centers. This list is designed to be consistent with the previous Eurocleft cephalometric studies, and also to provide a comprehensive assessment of craniofacial morphology with standard cephalometric measures that have been well established in orthodontics and for which there are norms available for comparison to unaffected controls.

TABLE I

Measurement	**Evaluator Initials____**
SNA (˚)	
SNB (˚)	
ANB (˚)	
Ba-N-ANS (˚)	
Ba-N-Pg (˚)	
ANS-N-Pg (˚)	
WITS appraisal (A┴OP:B┴OP) (mm)	
Ba-N (mm)	
PNS’-ANS (mm)	
Md length (Co-Gn) (mm)	
SN-MP (SN-GoGn) (˚)	

ANS-Me (mm)	
N-Me (mm)	
ANS-Me/N-Me (%)	
U1-PP (˚)	
L1-MP (L1-GoGn) (˚)	

5) ***Statistical Analysis -*** Statistical evaluation will be performed with *repeated-measures analysis of variance* comparing the *group means* for the different centers per measurement assessment and checking for an Institution effect, time effect, and time-Institution interaction. Variance terms will be included in the model to account for between-subject variation.

PUBLICATIONS

1. Daskalogiannakis J, Mercado AM, Russell KA, Hathaway RR, Dugas GS, Long Jr RE, Cohen MA, Semb G, Shaw W: The Americleft Study: An intercenter study of treatment outcomes for patients with unilateral cleft lip and palate. Part 3 – Analysis of craniofacial form. Cleft Palate-Craniofacial Journal, 48:252-258, 2011.

2. Kornbluth M, Campbell RE, Daskalogiannakis J, Ross EJ, Glick PH, Russell KA, Doucet JC, Hathaway RR, LongJr RE, Sitzman TJ. Active presurgical infant orthodpedics for unilateral cleft lip and palate: Intercenter outcome comparison of Latham, modified McNeil, and nasoalveolar molding. Cleft Palate Craniofacial J, 55:639-648, 2018.

3. Doucet JC, Russell KA, Daskalogiannakis J, Mercado A, Emanuele N, James L, Hathaway RR, LongJr RE. Facial growth of patients with complete unilateral cleft lip and palate treated with alveolar bone grafting at 6 years. Cleft Palate-Craniofac J, 56:619-657, 2019.

PRESENTATIONS

2010 ACPA Fort Worth, TX

CEPHALOMETRIC COMPARISON OF TREATMENT OUTCOME IN PATIENTS WITH CBCLP FROM 3 DIFFERENT CENTERS
Daskalogiannakis, Dugas, Long, Hathaway

2016 ACPA Atlanta, GA

THE AMERICLEFT PROJECT: FACIAL GROWTH IN UNILATERAL CLEFT LIP AND PALATE TREATED WITH ALVEOLAR BONE GRAFTING AT 6 YEARS: COMPARISON WITH EUROCLEFT DATA
Doucet, Russell, Daskalogiannakis, Emanuele, James, Mercado, Hathaway, Semb, Shaw, Long

THE AMERICLEFT PROJECT: FACIAL GROWTH IN UNILATERAL CLEFT LIP AND PALATE TREATED WITH ALVEOLAR BONE GRAFTING AT 6 YEARS: COMPARISON WITH AMERICLEFT DATA
Doucet, Russell, Daskalogiannakis, Emanuele, James, Glick, Kornbluth, Sitzman, Beals, Hathaway, Long